Claims

1. A product comprising a polynucleotide sequence encoding a toxin or prodrug-converting enzyme and a polynucleotide sequence encoding a stress response protein or an inducer of stress response protein expression.

2. The product of claim 1, for use in enhancing an immune response.

3. The product of either of claims 1 or 2 wherein the immune response enhanced is an anti-tumour response.

4. The product of any of claims 1 to 3 wherein the polynucleotide sequence encoding a toxin or prodrug-converting enzyme capable of inducing necrotic cell death and the polynucleotide sequence encoding a stress response protein or an inducer of stress response protein expression are both components of single polynucleotide molecule.

5. The product of any of claims 1 to 4 wherein the toxin or prodrug-converting enzyme is a nitroreductase capable of activating the prodrug CB1954.

6. The product of any of claims 1 to 4 wherein the toxin or prodrug-converting enzyme is a cytochrome P450.

7. The product of claim 5 wherein the cytochrome P450 is selected from the list consisting of human CYP1A2, human CYP2E1, human CYP3A4, rodent CYP1A2, rodent CYP2E1 and rodent CYP3A4.

8. The product of any of claims 1 to 7 wherein the stress response protein encoded or induced is a heat shock protein.

9. The product of claim 8 wherein the heat shock protein is selected from the list consisting of Hsp70, Hsp90, Hsp110, calreticulin, gp96, grp170, Hsp27, Hsc70, *Mycobacterium* Hsp65, *Legionella pneumophila* Hsp60, *Escherichia coli* GroEL and GroES.

10. The product of claim 9 wherein the heat shock protein is Hsp70.

11. A DNA vaccine comprising the product of any of claims 1–10.

12. A DNA vaccine comprising a polynucleotide encoding a toxin or prodrug-converting enzyme for enhancing an anti-tumour immune response.

13. The DNA vaccine of claim 12 wherein the toxin or prodrug-converting enzyme is a nitroreductase capable of activating the prodrug CB1954.

14. The DNA vaccine of claim 13 wherein the toxin or prodrug-converting enzyme is a cytochrome P450.

15. The DNA vaccine of claim 14 wherein the cytochrome P450 is selected from the list consisting of human CYP1A2, human CYP2E1, human CYP3A4, rodent CYP1A2, rodent CYP2E1 and rodent CYP3A4

16. A product comprising a polynucleotide encoding a nitroreductase capable of activating the prodrug CB1954 and a polynucleotide encoding an immunostimulatory molecule, for use in enhancing an anti-tumour immune response.

17. A product comprising a polynucleotide encoding a cytochrome P450 and a polynucleotide encoding an immunostimulatory molecule, for use in enhancing an anti-tumour immune response.

18. The product of either of claims 16 or 17 wherein the immunostimulatory molecule is selected from the list consisting of GM-CSF, IL-1, IL-2, IL-4, IL-6, IL-10, IL-12, IL-18, B7-2, TNFα, γ-IFN, MCP-1, MIP-2, RANTES, TGF-β, CD154, CD134 ligand, MHC Class I, MHC Class II, CD135 ligand and TRAIL.

19. A vector encoding and allowing expression of
a) a toxin or prodrug-converting enzyme and
b) a stress response protein,
for use in enhancing an immune response.

20. The vector of claim 19 wherein the immune response is an anti-tumour response.

21. The vector of either of claims 19 or 20 wherein the stress response protein is a heat shock protein.

22. The vector of claim 21 wherein the heat shock protein is selected from the list consisting of Hsp70, Hsp90, Hsp110, calreticulin, gp96, grp170, Hsp27, Hsc70, *Mycobacterium* Hsp65, *Legionella pneumophila* Hsp60, *Escherichia coli* GroEL and GroES.

23. The vector of claim 22 wherein the heat shock protein is hsp70.

24. The vector of any of claims 19 to 23 wherein the toxin or prodrug-converting enzyme is a nitroreductase capable of activating the prodrug CB1954.

25. The vector of any of claims 19 to 23 wherein the toxin or prodrug-converting enzyme is a cytochrome P450.

26. The vector of claim 25 wherein the cytochrome P450 is selected from the list consisting of human CYP1A2, human CYP2E1, human CYP3A4, rodent CYP1A2, rodent CYP2E1 and rodent CYP3A4.

27. The vector of any of claims 19 to 26 wherein one or both of the polynucleotide sequences encoding of the toxin or prodrug-converting enzyme on the one hand, and the stress response protein or inducer of stress protein expression on the other, operably linked to one or more promoters providing tumour-selective expression.

28. The vector of claim 27 wherein the promoter comprises one or more TCF-responsive elements.

29. The vector of any of claims 19 to 29 wherein the vector is a viral vector.

30. The vector of claim 29 wherein the vector is an adenoviral vector.

31. The vector of claim 29 wherein the vector is a retroviral vector.

32. The vector of claim 31 wherein the vector is a lentiviral vector.

33. An adenoviral vector encoding and allowing expression of
a) a nitroreductase capable of activating the prodrug CB1954 and
b) hsp70
for use in enhancing an anti-tumour immune response.

34. A host cell comprising the vector of any of claims 19 to 33.

35. A vaccine comprising the product of any of claims 1 to 10, or 16 to 18, the vector of any of claims 19 to 33, or the host cell of claim 34.

36. The product of any of claims 1 to 10, or 16 to 18, the DNA vaccine of any of claims 10 to 15, the vector of any of claims 19 to 33, or the host cell of claim 34 for use as a medicament.

37. The product of any of claims 1 to 10, or 16 to 18, the vector of any of claims 19 to 33, or the host cell of claim 34 for use as a vaccine.

38. A pharmaceutical composition comprising composition of any of claims 1 to 10, or 16 to 18, the DNA vaccine of any of claims 10 to 15, the vector of any of claims 19 to 33, or the host cell of claim 34 together with a pharmaceutically-acceptable diluent, buffer, adjuvant or excipient.

39. Use of the product of any of claims 1 to 10, or 16 to 18, the DNA vaccine of any of claims 10 to 15, the vector of any of claims 19 to 33, or the host cell of claim 34 for the manufacture of a medicament for the treatment of cancer.

40. Use of the product of any of claims 1 to 10, or 16 to 18, the DNA vaccine of any of claims 10 to 15, the vector of any of claims 19 to 33, or the host cell of claim 23 for the manufacture of a vaccine for the treatment of cancer.

41. A method of enhancing an immune response, comprising administering a therapeutic amount of a product comprising a polynucleotide encoding a toxin or prodrug-converting enzyme and a polynucleotide encoding a heat shock protein or an inducer of heat shock protein expression.

42. The method of claim 41, wherein the immune response is an anti-tumour immune response.

43. A method of treating a human suffering from a form of cancer, comprising administering a therapeutic amount of a product comprising a polynucleotide encoding a toxin or prodrug-converting enzyme and a polynucleotide encoding a heat shock protein or an inducer of heat shock protein expression.

44. The method of any of claims 41 to 43, comprising
    a) administering a therapeutic amount of a product comprising a polynucleotide encoding a nitroreductase capable of activating the prodrug CB1954 and a polynucleotide encoding a heat shock protein,
    b) allowing a period of time during which the product enters tumour cells and the encoded nitroreductase and heat shock protein are expressed, and
    c) administering a therapeutic amount of CB1954.

45. The method of any of claims 40 to 42, comprising
    a) administering a therapeutic amount of a product comprising a polynucleotide encoding a cytochrome P450 and a polynucleotide encoding a heat shock protein,
    b) allowing a period of time during which the product enters tumour cells and the encoded cytochrome P450 and heat shock protein are expressed, and
    c) administering a therapeutic amount of a prodrug.

46. The method of claim 43 wherein the prodrug is acetaminophen

47. The method of any of claims 40 to 44 wherein the heat shock protein is Hsp70.

48. A method of treating a human suffering from a form of cancer, comprising administering a therapeutic amount of a product comprising a polynucleotide encoding a heat shock protein, and a therapeutic amount of anti-cancer cytotoxic drug, such that a therapeutic anti-tumour immune response is induced.

49. A method of eliciting an anti-tumour immune response comprising

a) administering a therapeutic amount of a product comprising a polynucleotide encoding a nitroreductase capable of activating the prodrug CB1954,

b) allowing a period of time during which the composition enters tumour cells and the encoded nitroreductase is expressed, and

c) administering a therapeutic amount of CB1954.